

REMARKS

It is respectfully requested that this application be reconsidered in view of the above amendments and the following remarks and that all of the claims remaining be allowed.

Claims Amendments:

Claim 1 has been amended to recite that the multiple injections are performed on the same day. Support for this recitation can be found, for example, at Example 2 (particularly at page 21, lines 10-11).

No new matter has been added by these amendments. The Examiner is hereby requested to enter these amendments.

Applicants wish to point out that the amendments presented herein are made in the interest of expediting prosecution of the present application. Thus, Applicants submit that none of the claims now presented or previously presented are anticipated by or rendered obvious over the prior art.

Rejection Under 35 U.S.C. §102:

The rejection of claims 1-6, 8, 9 and 13-21 under 35 U.S.C. §102 as alleged being anticipated by Lee et al. (WO 99/08692) is obviated in part and traversed in part as set forth below.

The standard of anticipation under 35 U.S.C. §102 is that each and every element of the claim must be found in the cited reference. *In re Marshall*, 198 USPQ 344 (CCPA 1978).

Claim 1, as amended, is directed to a method for delivering a virus to a solid tumor to reduce growth of the tumor, comprising administering an effective amount of virus to a subject bearing the tumor, wherein the virus is capable of selectively killing tumor cells, by a base administration selected from the group consisting of:

- (a) delivering on the same day a composition comprising the virus to multiple sites inside the solid tumor; and
- (b) delivering directly into the tumor a composition comprising the virus, wherein the volume of the composition is between about 10% to about 100% of the volume of the tumor.

WO 99/08692 does not teach the delivery of a composition comprising the virus to multiple sites inside the solid tumor on the same day, as recited in alternative (a) in claim 1. Nor does WO 99/08692 teach the delivery of a volume between about 10% to about 100% of the volume of the tumor, as recited in alternative (b) in claim 1. The Office Action states that WO 99/08692 teaches an injection of 20 μ l into a tumor with an area of 0.31 cm², thereby teaching a delivery of 6.45% of the volume of the tumor. However, since WO 99/08692 merely discloses the surface area, rather than volume of the tumor, the percentage of delivered volume relative to the tumor volume can not be determined. Thus, WO 99/08692 does not teach any ratio between volume of the injected composition and the volume of the tumor.

Accordingly, WO 99/08692 does not teach each and every element of claim 1. Claims 2-6, 8, 9 and 13-21 all depend from claim 1, and therefore contain all the elements of claim 1. Consequently, WO 99/08692 likewise does not teach each and every element of claims 2-6, 8, 9 and 13-21. Therefore, the requirement under 35 U.S.C. §102 is not met, and withdrawal of this rejection is respectfully requested.

Rejection Under 35 U.S.C. §103:

1. The rejection of claims 1 and 7 under 35 U.S.C. §103(a) as allegedly being unpatentable over Lorence et al. (WO 94/25627) is respectfully traversed for the following reasons.

To properly issue a rejection under 35 U.S.C. §103, the USPTO bears the initial burden to establish a prima facie case of obviousness by meeting three criteria. First, there must be some suggestion or motivation, either in the references themselves or in the

knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings to arrive at the claimed invention. *In re Vaeck*, 20 USPQ 2d 1438 (Fed. Cir. 1991). Second, there must be a reasonable expectation of success. *Id.* Finally, the prior art reference or the combination of references must teach or suggest all the claim limitations. *In re Royka*, 180 USPQ 580 (CCPA 1974).

The present rejection does not meet any of these criteria. Claims 1 and 7 are directed to methods of administering a virus to multiple sites in a tumor on the same day, or in a volume between about 10% and 100% of the volume of the tumor. WO 94/25627 teaches administration of Newcastle Disease virus into tumors, but nowhere does it teach or suggest multiple injection in a tumor on the same day, or an injection volume between about 10% and 100% of the volume of the tumor. Clearly, a mere teaching of "[e]ffective dosages and schedules for administering the virus may be determined empirically" does not constitute teaching or suggestion of the specific claim elements of claim 1 or 7. In addition, a teaching regarding dosages can not be extended to the claim element of volume, let alone the ratio of the injection volume relative to the volume of the tumor, as required in claims 1 and 7. Furthermore, even if there is a motivation to devise the most effective dosage and schedule for administering a virus, WO 94/25627 does not teach or suggest how to arrive at the claimed invention, or a reasonable expectation of success of practicing the claimed invention.

Therefore, this rejection does not satisfy any of the required criteria under 35 U.S.C. §103, and its withdrawal is respectfully requested.

2. The rejection of claims 10-12 under 35 U.S.C. §103(a) as allegedly being unpatentable over Lee et al. (U.S. Patent No. 6,110,461; "the '461 patent") is respectfully traversed as set forth below.

Claim 10 is directed to a method for delivering a virus to a solid tumor to reduce growth of the tumor, wherein the virus is delivered to multiple sites inside the tumor on the same day, at one site per about 0.25 cubic centimeter of the tumor. Claims 11 and 12 are

directed to methods for delivering a virus to a solid tumor to reduce growth of the tumor, wherein the volume of the virus-containing composition is at least 30% and 50% of the volume of the tumor, respectively.

The Office Action states that the '461 patent teaches a course of 6 injections over 9 days and an injection of 20 μ l into a tumor with an area of 0.31 cm^2 . Citing *in re Aller*, 105 USPQ 233 (CCPA 1955), the Office Action alleges that it would have been *prima facie* obvious to perform routine optimization.

However, a particular parameter must first be recognized as a result-effective variable, i.e., a variable which achieves a recognized result, before the determination of the optimum of said variable might be characterized as routine experimentation. *In re Antonie*, 195 USPQ 6 (CCPA 1977). MPEP §2144.05, II.B. In *in re Antonie*, the invention was a water treatment device with a tank in which contactors continuously rotate. The primary prior art reference showed the device's basic structure but was silent regarding quantitative design parameters other than to give data on a single example. The claimed device has a ratio of tank volume to contactor area of at least about 0.12 gallon/ ft^2 , and the Patent Office rejected the claims on the ground of obviousness in view of the prior art reference. The Court of Customs and Patent Appeals reversed, noting:

"In *In re Aller*, 220 F.2d 454, 42 CCPA 824, 105 USPQ 233 (1955), the court set out the rule that the discovery of an optimum value of a variable in a known process is normally obvious. We have found exceptions to this rule... (omitted) This case, in which the parameter optimized was not recognized to be a result-effective variable, is another exception".

In re Antonie, 195 USPQ at 8-9.

Here, the '461 patent does not recognize that multiple injections in the same tumor mass on the same day, let alone an injection per about 0.25 cubic centimeter of the tumor, is a result-effective variable which can be used to optimize the result. The '461 patent also does not recognize the ratio of the injected volume to the volume of the tumor as a result-

effective variable. Therefore, under *in re Antonie*, the present case constitute an exception to the *in re Aller* rule.

Accordingly, the claimed invention is not obvious in view of the '461 patent, and withdrawal of the rejection is respectfully requested.


Conclusions:

For the reasons set forth above, Applicants submit that the claims of this application are patentable. Reconsideration and withdrawal of the Examiner's rejections are hereby requested. Allowance of the claims remaining in this application is earnestly solicited.

In the event that a telephone conversation could expedite the prosecution of this application, the Examiner is requested to call the undersigned at (650) 622-2340.

Respectfully submitted,

BURNS, DOANE, SWECKER & MATHIS, L.L.P.

By:  _____
Ping F. Hwang
Registration No. 44,164
Attorney for Applicants
Redwood Shores, CA Office
(650) 622-2300

P.O. Box 1404
Alexandria, Virginia 22313-1404
Date: May 24, 2002



Amendment and Reply to Office Action
Application No. 09/987,687
Attorney's Docket No. 032775-078

Page 1

Attachment to Amendment and Reply dated May 24, 2002

Marked-up Copy
Claims

RECEIVED

MAY 29 2002

TECH CENTER 1600/2300

1. (amended) A method for delivering a virus to a solid tumor to reduce growth of the tumor, comprising administering an effective amount of virus to a subject bearing the tumor, wherein the virus is capable of selectively killing tumor cells, by a base administration selected from the group consisting of:
 - (a) delivering on the same day a composition comprising the virus to multiple sites inside the solid tumor; and
 - (b) delivering directly into the tumor a composition comprising the virus, wherein the volume of the composition is between about 10% to about 100% of the volume of the tumor.